

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of

BANTICK et al

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Group:

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Examiner:

For: NOVEL COMPOUNDS

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February 14, 2002

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**PRELIMINARY AMENDMENT**

Please amend the above-identified application as follows:

**IN THE CLAIMS**

Please substitute the following amended claims for corresponding claims previously presented. A copy of the amended claims showing current revisions is attached.

3. (Amended) A compound of formula I, as defined in Claim 1-, wherein R<sup>4</sup> represents H or C<sub>1-6</sub> alkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

4. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>1</sup> represents C<sub>1-6</sub> alkyl or C<sub>4-6</sub> cycloalkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

5. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>4</sup> and R<sup>5</sup> together represent pyrrolidinyl when R<sup>1</sup> represents A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

6. (Amended) A compound of formula I, as defined in claim 2, wherein A<sup>1</sup> represents C<sub>1-3</sub> alkylene, and R<sup>4</sup> represents H or C<sub>1-3</sub> alkyl and R<sup>5</sup> represents C<sub>2-6</sub> alkyl or C<sub>5-6</sub> cycloalkyl, or R<sup>4</sup> and R<sup>5</sup> together represent pyrrolidinyl.

8. (Amended) A compound of formula I, as defined in Claim 1 , wherein R<sup>4</sup> represents C<sub>1-6</sub> alkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)OR<sup>4</sup>.

9. (Amended) A compound of formula I, as defined in Claim 7 , wherein A<sup>1</sup> represents C<sub>1-5</sub> alkylene and R<sup>4</sup> represents C<sub>1-4</sub> alkyl.

11. (Amended) A compound as claimed in Claim 1 , wherein R<sup>3</sup> represents H, linear C<sub>1-10</sub> alkyl, branched C<sub>3-10</sub> alkyl, partially cyclic C<sub>4-10</sub> alkyl, C<sub>4-10</sub> cycloalkyl, optionally substituted linear C<sub>1-3</sub> alkylphenyl, optionally substituted branched C<sub>3</sub> alkylphenyl.

13.. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>2</sup>

represents OH.

14. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>6</sup> represents optionally substituted phenyl or C<sub>1-17</sub> alkyl (which latter group may be linear or, when there are a sufficient number of carbon atoms, may be branched, be cyclic or partially cyclic, and/or be saturated or unsaturated) when R<sup>2</sup> represents OC(O)R<sup>6</sup>.

17. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>7</sup> represents optionally substituted phenyl, C<sub>1-12</sub> alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched, cyclic or partially cyclic, and/or saturated or unsaturated), or C<sub>1-3</sub> alkylphenyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched) when R<sup>2</sup> represents C(O)OR<sup>7</sup>.

20. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>8</sup> represents H or methyl, when R<sup>2</sup> represents C(O)OCH(R<sup>8</sup>)OC(O)R<sup>9</sup>.

21. (Amended) A compound of formula I, as defined in claim 1, wherein R<sup>9</sup> represents phenyl, or C<sub>1-8</sub> alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched and/or cyclic or partially cyclic) when R<sup>2</sup> represents C(O)OCH(R<sup>8</sup>)OC(O)R<sup>9</sup>.

22.. (Amended) A compound of formula I, as defined in claim 20 wherein R<sup>8</sup> represents H or methyl and R<sup>9</sup> represents phenyl, C<sub>5-7</sub> cycloalkyl, linear C<sub>1-6</sub> alkyl, branched C<sub>3-6</sub> alkyl or partially cyclic C<sub>7-8</sub> alkyl.

24. (Amended) A compound as claimed in claim 1 wherein, when R<sup>1</sup> represents R<sup>3</sup> and R<sup>3</sup> represents optionally substituted C<sub>1-3</sub> alkylphenyl, the optional substituent C<sub>1-4</sub> alkyl.

26. (Amended) A compound as claimed in claim 1 wherein, when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted C<sub>1-12</sub> alkyl, the optional substituent is selected from halogen and C<sub>1-6</sub> alkoxy..

28. (Amended) A compound as claimed in claim 1 wherein, when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted phenyl, the optional substituent is selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy and halogen..

30. (Amended) A compound as claimed in wherein when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted C<sub>1-3</sub> alkylphenyl, the optional substituent is nitro.

39. (Amended) A pharmaceutical formulation including a compound of formula I

as defined in claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

40. (Amended) A compound of formula I, as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

41. (Amended) A compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of -a condition where inhibition of thrombin is required..

42.. (Amended) A compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of thrombosis.

43. (Amended) A compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

44.. (Amended) The use of a compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

46. (Amended) The use of a compound of formula I as defined in claim 1 , or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an

anticoagulant..

47. (Amended) A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

**REMARKS**

The above amendments have been made to place the application in a more traditional format. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made.**"

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS**

3. (Amended) A compound of formula I, as defined in Claim 1.[or Claim 2], wherein R<sup>4</sup> represents H or C<sub>1-6</sub> alkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

4. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 3] claim 1, wherein R<sup>1</sup> represents C<sub>1-6</sub> alkyl or C<sub>4-6</sub> cycloalkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

5. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 3] claim 1, wherein R<sup>4</sup> and R<sup>5</sup> together represent pyrrolidinyl when R<sup>1</sup> represents A<sup>1</sup>C(O)N(R<sup>4</sup>)R<sup>5</sup>.

6. (Amended) A compound of formula I, as defined in [any one of Claims 2 to 5] claim 2, wherein A<sup>1</sup> represents C<sub>1-3</sub> alkylene, and R<sup>4</sup> represents H or C<sub>1-3</sub> alkyl and R<sup>5</sup> represents C<sub>2-6</sub> alkyl or C<sub>5-6</sub> cycloalkyl, or R<sup>4</sup> and R<sup>5</sup> together represent pyrrolidinyl.

8. (Amended) A compound of formula I, as defined in Claim 1 [or Claim 7], wherein R<sup>4</sup> represents C<sub>1-6</sub> alkyl when R<sup>1</sup> represents -A<sup>1</sup>C(O)OR<sup>4</sup>.

9. (Amended) A compound of formula I, as defined in Claim 7 [or Claim 8], wherein A<sup>1</sup> represents C<sub>1-5</sub> alkylene and R<sup>4</sup> represents C<sub>1-4</sub> alkyl.

11. (Amended) A compound as claimed in Claim 1 [or Claim 10], wherein R<sup>3</sup> represents H, linear C<sub>1-10</sub> alkyl, branched C<sub>3-10</sub> alkyl, partially cyclic C<sub>4-10</sub> alkyl, C<sub>4-10</sub> cycloalkyl, optionally substituted linear C<sub>1-3</sub> alkylphenyl, optionally substituted branched C<sub>3</sub> alkylphenyl.

13.. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R<sup>2</sup> represents OH.

14. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R<sup>6</sup> represents optionally substituted phenyl or C<sub>1-17</sub> alkyl (which latter group may be linear or, when there are a sufficient number of carbon atoms, may be branched, be cyclic or partially cyclic, and/or be saturated or unsaturated) when R<sup>2</sup> represents OC(O)R<sup>6</sup>.

17. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R<sup>7</sup> represents optionally substituted phenyl, C<sub>1-12</sub> alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched, cyclic or partially cyclic, and/or saturated or unsaturated), or C<sub>1-3</sub> alkylphenyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched) when R<sup>2</sup> represents C(O)OR<sup>7</sup>.

20. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12] claim 1, wherein R<sup>8</sup> represents H or methyl, when R<sup>2</sup> represents C(O)OCH(R<sup>8</sup>)OC(O)R<sup>9</sup>.

21. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 12 or Claim 20] claim 1, wherein R<sup>9</sup> represents phenyl, or C<sub>1-8</sub>, alkyl (which latter group is optionally substituted, may be linear or, when there are a sufficient number of carbon atoms, may be branched and/or cyclic or partially cyclic) when R<sup>2</sup> represents C(O)OCH(R<sup>8</sup>)OC(O)R<sup>9</sup>.

22.. (Amended) A compound of formula I, as defined in [Claim 20 or Claim 21] claim 20 wherein R<sup>8</sup> represents H or methyl and R<sup>9</sup> represents phenyl, C<sub>5-7</sub> cycloalkyl, linear C<sub>1-6</sub> alkyl, branched C<sub>3-6</sub> alkyl or partially cyclic C<sub>7-8</sub> alkyl.

24. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R<sup>1</sup> represents R<sup>3</sup> and R<sup>3</sup> represents optionally substituted C<sub>1-3</sub> alkylphenyl, the optional substituent C<sub>1-4</sub> alkyl.

26. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted C<sub>1-12</sub> alkyl, the optional substituent is selected from halogen and C<sub>1-6</sub> alkoxy..

28. (Amended) A compound as claimed in [any one of the preceding claims] claim 1 wherein, when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted phenyl, the optional substituent is selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy and halogen..

30. (Amended) A compound as claimed in [any one of the preceding claims] wherein when R<sup>2</sup> represents C(O)OR<sup>7</sup> and R<sup>7</sup> represents optionally substituted C<sub>1-3</sub> alkylphenyl, the optional substituent is nitro.

39. (Amended) A pharmaceutical formulation including a compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

40. (Amended) A compound of formula I, as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

41. (Amended) A compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of - a condition where inhibition of thrombin is required..

42.. (Amended) A compound of formula I as defined in [any one of Claims 1 to

38] claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of thrombosis.

43. (Amended) A compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

44.. (Amended) The use of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

46. (Amended) The use of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1 , or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an anticoagulant..

47. (Amended) A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound of formula I as defined in [any one of Claims 1 to 38] claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.